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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,442	04/13/2001	John S. Whitaker	29342/37225	2950

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EXAMINER	
BAHAR, MOJDEH	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/834,442	Applicant(s) WHITAKER ET AL.	
	Examiner Mojdeh Bahar	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-11,13 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-11,13 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daugan et al. (WO 96/32003).

Daugan et al. (WO 96/32003) teaches a pharmaceutical composition comprising a PDE-5 inhibitor compound of formula I, see abstract. Daugan et al. (WO 96/32003) teaches that its pharmaceutical composition can be used to treat erectile dysfunction, see particularly page 7, line 34 and page 8 line 1. Daugan et al. (WO 96/32003) shows that the compounds of formula I exhibit an IC50 value of less than 10 nM, see particularly Table 1. Daugan et al. (WO 96/32003) also teaches that the preferred route of administration is oral, and that the dosage range is from 0.5-800 mg, individual tablets contain from 0.2-400 mg of the active compound in a suitable pharmaceutically acceptable carrier, for administration in single or multiple doses, once or several times per day (which may constitute chronic administration), see particularly page 9, lines 5-11. Daugan et al. (WO 96/32003) also teaches that its pharmaceutical composition can be used in treating cardiovascular disorders, e.g. conditions of reduced blood vessel patency, peripheral vascular disease, see particularly page 7, lines 21 to page 8, line 2.

Daugan et al. (WO 96/32003) does not teach the inclusion of a package insert or a container.

It would have been obvious to one of ordinary skill at the time the invention was made to include the PDE-5 active herein in a container and to include the package insert herein for the therapeutic composition.

One of ordinary skill in the art would have been motivated to include the therapeutic agent comprising PDE5 in a container since the packaging of pharmaceutical compositions is widely practiced in the art and is therefore within the skill of the artisan. Moreover, the inclusion of a package insert including "indications and use" of the pharmaceutical composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art. (See *Remington's: the Science and Practice of Pharmacy*, Nineteenth Edition, Vol. 1, page 806).

Claims 1-2, 5-11,13, 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daugan WO 97/03675 (submitted by the applicant in the parent application 09/558911, August 29, 2001), and *Remington: The Science and Practice of Pharmacy* (of record in the previous office action).

Daugan teaches compounds of formula I (which reads on formula I of the instant application) in general and the two particular compounds recited in claim 10 herein in an article useful in treating erectile dysfunction in a dose of 0.5-800 mg/day, see abstract, claim 4 and page 5 in particular. Daugan also teaches that its composition can be administered in single or multiple doses, once or several times a day, see page 5.

WO 97/03675 does not teach the inclusion of a package insert, nor does it disclose a container.

It would have been obvious to one of ordinary skill at the time the invention was made to include the PDE-5 actives herein in a container and to include the package insert herein for the therapeutic composition.

One of ordinary skill in the art would have been motivated to include the therapeutic agent comprising PDE5 herein in a container since the packaging of pharmaceutical compositions in articles is widely practiced in the art and is therefore within the skill of the artisan. Moreover, the inclusion of a package insert including "indications and use" of the pharmaceutical composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art. (See *Remington's: the Science and Practice of Pharmacy*, Nineteenth Edition, Vol. 1, page 806).

Response to Arguments

Applicant's arguments with respect to the chronic dosage regimen herein have been considered, but are not persuasive. Applicant fist argues that an IC50 value of less than 10nM alone is not sufficient to render a compound suitable for use in the present invention. Applicant further states that the PDE5 inhibitor must also have a sufficient bioavailability to be effective in about 1-10 mg unit oral dosage forms. Note that the prior art reference, Daugan '003, teaches tablets containing between 0.2-400 mg of active indicating that the compounds herein have sufficient bioavailability even at 0.2 mg, see page 9, lines 5-11.

Applicant argues that the claimed invention differs from the cited prior art in that the instant invention requires a chronic dosage regimen. Note that the cited references broadly teach that their compositions can be administered in single or multiple doses, once or several times a

day. As set forth in the last office action in the section entitled Response to Arguments, the teaching of the prior art (specifically '675 patent) is not an on-demand regimen, contrary to the applicant's assertion. Applicant *assumes* that the regimen in the prior art is a one- day regimen. Nowhere does the prior art indicate that its regimen is a one-day regimen. In fact the prior art teaches the treatment of many chronic diseases, e.g., COPD, hypertension, inflammatory diseases, for which a one-day therapeutic regimen is not routinely prescribed, see in particular page 8 of '003.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant then argues that the printed material on the package insert should be given patentable weight. Applicant argues that the instant case is analogous to the *In re Miller* 164 USPQ 46 (CCPA1969) and *In re Gulack* 217 USPQ 401 (CAFC) 1983. Note that the *Miller* Court relies on the fact that there is a functional relationship between a measuring cup and the indicia (printed material) on the cup. A cup is not a measuring cup without the indicia since one cannot employ the cup (without indicia) to take accurate measurements. The instant case is distinguishable from *Miller* since a patient can take a medication even without having the instructions at hand. The ultimate function of the instant article of manufacture relies not on the instructions, but on the active pharmaceutical ingredient, i.e., the PDE5 inhibitor, contained therein.

The Court in *In re Gulack* also states that "where the printed material is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." Here, the set of instructions is not functionally related to the article of manufacture because the article of manufacture can function as an active and effective drug even in the absence of the set of instructions (i.e., package insert). Therefore following the reasoning in *Miller* and *Gulack*, we can conclude that the "printed material", i.e., the package insert, does not patentably distinguish the instant claims over the prior art. Note that the logical conclusion of the applicant's argument as to the patentable weight of the package insert would yield the following: an old drug claimed in a kit along with a new set of instructions makes the kit claim patentable merely because of the printed material on the insert.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
April 4, 2003

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

12/1/03